(FILE 'HOME' ENTERED AT 11:28:18 ON 22 JAN 2001)

FILE 'MEDLINE, CAPLUS, BIOSIS' ENTERED AT 11:28:34 ON 22 JAN 2001

L1	223	S	(MELANOCORTIN)AND (5-RECEPTOR OR 2-RECEPTOR OR MC2 OR MC5 OR
L2	18	S	L1 AND (WEIGHT OR OBESE OR OBESITY OR OVERWEIGHT)
L3	13	DUP REM	L2 (5 DUPLICATES REMOVED)
L4	9	S	L3 NOT PY>1999
		E	BRENNAN M/AU
L5	0	S	E3 AND E5
L6	346	S	E3 OR E5
		E	BRENNAN MILES/AU
L7	26	S	E3-E5
		E	BRENNEN M B/AU
L8	372	S	L6 OR L7
L9	4	S	L8 AND (MELANOCORTIN OR MELANOCYTE)
L10	4	S	L9 NOT L3

ordered 1/22/04

L3 ANSWER 1 OF 13 CAPLUS COPYRIGHT 2001 ACS
TI HP-228 (Trega Biosciences Inc)
AU Wilkison, William O.
SO Curr. Opin. Cent. Peripher. Nerv. Syst. Invest. Drugs (2000), 2(2), 235-240
CODEN: COCDFA; ISSN: 1464-844X

L3 ANSWER 2 OF 13 BIOSIS COPYRIGHT 2001 BIOSIS
TI Novel selective ligands for the ***melanocortin*** -4 receptor. Their potential in the treatment of eating disorders.
AU Schioth, Helgi B. (1)
SO Regulatory Peptides., (Jan. 29, 2000) Vol. 86, No. 1-3, pp. 39. Meeting Info.: 21st Annual Winter Neuropeptide Conference. Breckenridge, Colorado, USA January 29-February 01, 2000 Cephalon, Inc . ISSN: 0167-0115.

L3 ANSWER 3 OF 13 CAPLUS COPYRIGHT 2001 ACS
TI MC3-R as a novel target for antiinflammatory therapy
AU Getting, Stephen J.; Perretti, Mauro
SO Drug News Perspect. (2000), 13(1), 19-27
CODEN: DNPEED; ISSN: 0214-0934

L3 ANSWER 4 OF 13 BIOSIS COPYRIGHT 2001 BIOSIS
TI Feeding behavior in rats chronically treated with ***melanocortin*** agonist, MTII.
AU Stair, J. N. (1); Shu, J. (1); Camacho, R. (1); Murphy, B. (1); Hickey, G. J. (1); MacIntyre, D. E. (1); Strack, A. M. (1)
SO Society for Neuroscience Abstracts., (1999) Vol. 25, No. 1-2, pp. 619. Meeting Info.: 29th Annual Meeting of the Society for Neuroscience. Miami Beach, Florida, USA October 23-28, 1999 Society for Neuroscience . ISSN: 0190-5295.

L3 ANSWER 5 OF 13 BIOSIS COPYRIGHT 2001 BIOSIS
TI Decreased dominant behavior and pheromonal signaling in ***melanocortin*** type- ***5*** ***receptor*** -deficient mice.
AU Morgan, C. (1); Thomas, R. E. (1); Ma, W.; Cepoi, D. (1); Novotny, M.; Cone, R. D. (1)
SO Society for Neuroscience Abstracts., (1999) Vol. 25, No. 1-2, pp. 605. Meeting Info.: 29th Annual Meeting of the Society for Neuroscience. Miami Beach, Florida, USA October 23-28, 1999 Society for Neuroscience . ISSN: 0190-5295.

L3 ANSWER 6 OF 13 BIOSIS COPYRIGHT 2001 BIOSIS
TI ***Melanocortin*** receptors: Perspectives for novel drugs.
AU Wikberg, Jarl E. S. (1)
SO European Journal of Pharmacology, (June 30, 1999) Vol. 375, No. 1-3, pp. 295-310.
ISSN: 0014-2999.

L3 ANSWER 7 OF 13 MEDLINE
TI Absence of genetic variation in some ***obesity*** candidate genes (GLP1R, ASIP, MC4R, MC5R) among Pima indians.
AU Norman R A; Permana P; Tanizawa Y; Ravussin E
SO INTERNATIONAL JOURNAL OF OBESITY AND RELATED METABOLIC DISORDERS, (1999 Feb) 23 (2) 163-5.
Journal code: BTX. ISSN: 0307-0565.

L3 ANSWER 8 OF 13 MEDLINE DUPLICATE 1
TI Long term orexigenic effect of a novel ***melanocortin*** 4 receptor selective antagonist.
AU Skuladottir G V; Jonsson L; Skarphedinsson J O; Mutulis F; Muceniece R; Raine A; Mutule I; Helgason J; Prusis P; Wikberg J E; Schioth H B
SO BRITISH JOURNAL OF PHARMACOLOGY, (1999 Jan) 126 (1) 27-34.
Journal code: B00. ISSN: 0007-1188.

L3 ANSWER 10 OF 13 MEDLINE
TI Linkage and association studies between the ***melanocortin*** receptors 4 and 5 genes and ***obesity*** -related phenotypes in the Quebec Family Study.
AU Chagnon Y C; Chen W J; Perusse L; Chagnon M; Nadeau A; Wilkison W O; Bouchard C
SO MOLECULAR MEDICINE, (1997 Oct) 3 (10) 663-73.
Journal code: CG3. ISSN: 1076-1551.

L3 ANSWER 11 OF 13 MEDLINE DUPLICATE 2
TI ART (protein product of agouti-related transcript) as an antagonist of MC-3 and MC-4 receptors.
AU Fong T M; Mao C; MacNeil T; Kalyani R; Smith T; Weinberg D; Tota M R; Van der Ploeg L H
SO BIOCHEMICAL AND BIOPHYSICAL RESEARCH COMMUNICATIONS, (1997 Aug 28) 237 (3) 629-31.
Journal code: 9Y8. ISSN: 0006-291X.

L3 ANSWER 12 OF 13 CAPLUS COPYRIGHT 2001 ACS
TI Receptor biology of the melanocortins, a family of neuroimmunomodulatory peptides
AU Tatro, Jeffrey B.
SO NeuroImmunoModulation (1997), Volume Date 1996, 3(5), 259-284
CODEN: NROIEM; ISSN: 1021-7401

L3 ANSWER 13 OF 13 MEDLINE DUPLICATE 3
TI Receptor biology of the melanocortins, a family of neuroimmunomodulatory peptides.
AU Tatro J B
SO NEUROIMMUNOMODULATION, (1996 Sep-Oct) 3 (5) 259-84. Ref: 224
Journal code: CCL. ISSN: 1021-7401.
L10 ANSWER 1 OF 4 MEDLINE
TI Obesity in the mouse model of pro-opiomelanocortin deficiency responds to peripheral ***melanocortin*** [see comments].
AU Yaswen L; Diehl N; ***Brennan M B*** ; Hochgeschwender U
SO NATURE MEDICINE, (1999 Sep) 5 (9) 1066-70.
Journal code: CG5. ISSN: 1078-8956.

L10 ANSWER 3 OF 4 CAPLUS COPYRIGHT 2001 ACS
TI Obesity in the mouse model of pro-opiomelanocortin deficiency responds to peripheral ***melanocortin***
AU Yaswen, Linda; Diehl, Nicole; ***Brennan, Miles B.*** ; Hochgeschwender, Ute
SO Nat. Med. (N. Y.) (1999), 5(9), 1066-1070
CODEN: NAMEFI; ISSN: 1078-8956

L10 ANSWER 4 OF 4 BIOSIS COPYRIGHT 2001 BIOSIS
TI Obesity in the mouse model of pro-opiomelanocortin deficiency responds to peripheral ***melanocortin*** .
AU Yaswen, Linda; Diehl, Nicole; ***Brennan, Miles B.*** ; Hochgeschwender, Ute (1)
SO Nature Medicine, (Sept., 1999) Vol. 5, No. 9, pp. 1066-1070. ISSN: 1078-8956.

L10 ANSWER 2 OF 4 CAPLUS COPYRIGHT 2001 ACS
AN 2000:401591 CAPLUS
DN 133:38707
TI Composition and method for regulation of body weight and associated conditions by administering proopiomelanocortin peptides or analogs thereof
IN ***Brennan, Miles B.*** ; Hochgeschwender, Ute
PA Eleanor Roosevelt Institute, USA; Oklahoma Medical Research Foundation
SO PCT Int. Appl., 168 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000033658	A1	20000615	WO 1999-US29337	19991209

W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

PRAI US 1998-111581 19981209
US 1999-146299 19990729
US 1999-146300 19990729
US 1999-146301 19990729
US 1999-146302 19990729
US 1999-146303 19990729
US 1999-146304 19990729
US 1999-146305 19990729
US 1999-146306 19990729
US 1999-374827 19990812
OS MARPAT 133:38707
RE.CNT 10
RE
(2) Eichhorn; Peptides 1995, V16(4), P665 CAPLUS
(4) Krude; Nat Gent 1998, V19(2), P155 CAPLUS
(5) Millennium Pharmaceuticas; WO 9747316 A1 1997, P82 CAPLUS
(7) Richter; Metab Clin Exp 1985, V34(6), P539 CAPLUS
(8) Wessells; Journal of Urology 1998, V160(2), P389 CAPLUS
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 9 OF 13 CAPLUS COPYRIGHT 2001 ACS
AN 1998:604932 CAPLUS
DN 129:216921
TI MSH-receptor subtype selective cyclic peptides
IN Wikberg, Jarl; Muceniece, Ruta; Mutulis, Felikss; Prusis, Peteris; Schioth, Helgi-birgir
PA Wapharm AB, Swed.
SO PCT Int. Appl., 57 pp.
CODEN: PIXXD2
DT Patent

LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 9837097	A1	19980827	WO 1998-SE270	19980216
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, GW, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
AU 9861274	A1	19980909	AU 1998-61274	19980216
EP 1025127	A1	20000809	EP 1998-905907	19980216
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
PRAI SE 1997-620		19970221		
WO 1998-SE270		19980216		

OS MARPAT 129:216921

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=> s MC2-R or MC5-R or melanocortin 2-receptor or melanocortin 5-receptor
        115 MC2
     195688 R
         12 MC2-R
            (MC2(W)R)
        108 MC5
     195688 R
         12 MC5-R
            (MC5(W)R)
        591 MELANOCORTIN
        140 MELANOCORTINS
        632 MELANOCORTIN
            (MELANOCORTIN OR MELANOCORTINS)
    2222142 2
     353161 RECEPTOR
     401747 RECEPTORS
     511577 RECEPTOR
            (RECEPTOR OR RECEPTORS)
          6 MELANOCORTIN 2-RECEPTOR
            (MELANOCORTIN(W)2(W)RECEPTOR)
        591 MELANOCORTIN
        140 MELANOCORTINS
        632 MELANOCORTIN
            (MELANOCORTIN OR MELANOCORTINS)
    1552741 5
     353161 RECEPTOR
     401747 RECEPTORS
     511577 RECEPTOR
            (RECEPTOR OR RECEPTORS)
         35 MELANOCORTIN 5-RECEPTOR
            (MELANOCORTIN(W)5(W)RECEPTOR)
L1       54 MC2-R OR MC5-R OR MELANOCORTIN 2-RECEPTOR OR MELANOCORTIN 5-
RECE
           PTOR

=> s l1 and expression
     446038 EXPRESSION
       8103 EXPRESSIONS
     450116 EXPRESSION
            (EXPRESSION OR EXPRESSIONS)
L2       21 L1 AND EXPRESSION

=> duplicate remove
ENTER L# LIST OR (END):l2
PROCESSING COMPLETED FOR L2
L3       21 DUPLICATE REMOVE L2 (0 DUPLICATES REMOVED)

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YOU HAVE REQUESTED DATA FROM 21 ANSWERS - CONTINUE? Y/(N):y

L3  ANSWER 1 OF 21  MEDLINE
ACCESSION NUMBER:  2001228121    MEDLINE
DOCUMENT NUMBER:  21139738  PubMed ID: 11243846
TITLE:             ***Expression***  of the  ***melanocortin***
                ***5***    ***receptor***  on rat lymphocytes.
```

AUTHOR: Akbulut S; Byersdorfer C A; Larsen C P; Zimmer S L; Humphreys T D; Clarke B L
CORPORATE SOURCE: Department of Medical Microbiology and Immunology, University of Minnesota-Duluth, Duluth, Minnesota, 55812, USA.
SOURCE: BIOCHEMICAL AND BIOPHYSICAL RESEARCH COMMUNICATIONS, (2001 Mar16) 281 (5) 1086-92.
Journal code: 9Y8; 0372516. ISSN: 0006-291X.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200104
ENTRY DATE: Entered STN: 20010502
Last Updated on STN: 20010502
Entered PubMed: 20010313
Entered Medline: 20010426

AB The ***expression*** of ***melanocortin*** - ***5*** ***receptor*** (***MC5*** - ***R***) mRNA and protein was characterized from isolated rat lymphocytes. The presence of ***MC5*** - ***R*** mRNA in spleen and thymus tissues was demonstrated by RT-PCR. The RT-PCR product was sequenced to confirm the identification of ***MC5*** - ***R*** . Tissues from lachrymal glands, adipose, adrenals, thymus, pancreas, and isolated splenic lymphocytes were detergent solubilized. The crude proteins were resolved by SDS-PAGE, transblotted to a nitrocellulose membrane, and probed for ***MC5*** - ***R*** using anti-receptor rabbit antisera. Two different types of polyclonal rabbit antisera were raised against synthetic peptides representing epitopes found at the amino (alphaN- ***MC5*** - ***R***) and the carboxyl termini (alphaC- ***MC5*** - ***R***) on the ***MC5*** - ***R*** . A prominent band at 77,000 (p77) was detected in all tissues except the pancreas. Preimmune sera did not detect p77 by Western analysis and the addition of peptide antigen neutralized the detection of p77 by the specific antisera. The receptor protein was purified from spleen and thymic lymphocytes using protein A agarose that precipitated material complexed to alphaN- ***MC5*** - ***R*** . The purified ***MC5*** - ***R*** was detected by Western analysis using alphaC- ***MC5*** - ***R*** . Both anti-receptor antisera, alphaN- ***MC5*** - ***R*** and alphaC- ***MC5*** - ***R*** , detected the p77. The p77 was treated with protein endoglycosidase F to produce a smaller protein band between 34-38,000 (p35); the inferred size is 37,000 based on the cDNA sequence. The data suggest that Asn-linked carbohydrate groups account for much of the p77 mass of the ***MC5*** - ***R*** . The data also demonstrate the ***expression*** of ***MC5*** - ***R*** protein on rat lymphocytes, thus, supporting the hypothesis that ***MC5*** - ***R*** is the ACTH receptor on lymphocytes. Copyright 2001 Academic Press.

L3 ANSWER 2 OF 21 MEDLINE
ACCESSION NUMBER: 2001200466 MEDLINE
DOCUMENT NUMBER: 21184529 PubMed ID: 11286624
TITLE: ***Expression*** , candidate gene, and population studies of the ***melanocortin*** ***5*** ***receptor*** .
AUTHOR: Hatta N; Dixon C; Ray A J; Phillips S R; Cunliffe W J; Dale M; Todd C; Meggit S; Birch-MacHin M A; Rees J L

CORPORATE SOURCE: Department of Dermatology, University of Newcastle upon Tyne, Newcastle upon Tyne, UK.
SOURCE: JOURNAL OF INVESTIGATIVE DERMATOLOGY, (2001 Apr) 116 (4) 564-70.
Journal code: IHZ; 0426720. ISSN: 0022-202X.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200105
ENTRY DATE: Entered STN: 20010517
Last Updated on STN: 20010517
Entered PubMed: 20010405
Entered Medline: 20010510

AB In mouse the ***melanocortin*** ***5*** ***receptor*** is known to regulate sebaceous gland function. To clarify its role in man, we have studied ***melanocortin*** ***5*** ***receptor*** ***expression*** in skin, and allelic variation at the ***melanocortin*** ***5*** ***receptor*** locus in diverse human populations and candidate disease groups. ***Melanocortin*** ***5*** ***receptor*** protein and mRNA ***expression*** were studied by immunohistochemistry and reverse transcriptase polymerase chain reaction. ***Melanocortin*** ***5*** ***receptor*** mRNA was detected in normal skin and cultured keratinocytes but not in cultured fibroblasts or melanocytes. Immunohistochemistry revealed ***melanocortin*** ***5*** ***receptor*** immunoreactivity in the epithelium and appendages, including the sebaceous gland, eccrine glands, and apocrine glands, as well as low level ***expression*** in the interfollciular epidermis. In order to screen for genetic diversity in the ***melanocortin*** ***5*** ***receptor*** that might be useful for allelic association studies we sequenced the entire ***melanocortin*** ***5*** ***receptor*** coding region in a range of human populations. One nonsynonymous change (Phe209Leu) and four synonymous changes (Ala81Ala, Asp108Asp, Ser125Ser, and Thr248Thr) were identified. Similar results were found in each of the populations except for the Inuit in which only the Asp108Asp variant was seen. The apparent "global distribution" of ***melanocortin*** ***5*** ***receptor*** variants may indicate that they are old in evolutionary terms. Variation of ***melanocortin*** ***5*** ***receptor*** was examined in patients with acne (n = 21), hidradenitis supprativa (n = 4), and sebaceous gland lesions comprising sebaceous nevi, adenomas, and hyperplasia (n = 13). No additional mutations were found. In order to determine the functional status of the Phe209Leu change, increase in cAMP in response to stimulation with alpha-melanocyte-stimulating hormone was measured in HEK-293 cells transfected with either wild-type or the Phe209Leu variant. The variant ***melanocortin*** ***5*** ***receptor*** was shown to act in a concentration-dependent manner, which did not differ from that of wild type. We have therefore found no evidence of a causative role for ***melanocortin*** ***5*** ***receptor*** in sebaceous gland dysfunction, and in the absence of any association between variation at the locus and disease group, the pathophysiologic role of the ***melanocortin*** ***5*** ***receptor*** in man requires further study.

L3 ANSWER 3 OF 21 MEDLINE
ACCESSION NUMBER: 2000231259 MEDLINE

DOCUMENT NUMBER: 20231259 PubMed ID: 10770490
TITLE: Impaired steroidogenic factor 1 (NR5A1) activity in mutant Y1 mouse adrenocortical tumor cells.
AUTHOR: Frigeri C; Tsao J; Czerwinski W; Schimmer B P
CORPORATE SOURCE: Banting and Best Department of Medical Research, University of Toronto, Ontario, Canada.
SOURCE: MOLECULAR ENDOCRINOLOGY, (2000 Apr) 14 (4) 535-44. Journal code: NGZ; 8801431. ISSN: 0888-8809.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200006
ENTRY DATE: Entered STN: 20000616
Last Updated on STN: 20000616
Entered Medline: 20000608

AB Mutants isolated from the Y1 mouse adrenocortical tumor cell line (clones 10r-9 and 10r-6) are resistant to ACTH because they fail to express the ***melanocortin*** - ***2*** ***receptor*** (MC2R). In this study, we show that a luciferase reporter plasmid driven by 1,800 bp of the proximal promoter region of the MC2R was expressed poorly in the mutant cells compared with parent Y1 cells. The differential ***expression*** of the MC2R in parent and mutant cells resulted from impaired activity of the orphan nuclear receptor NR5A1 (SF1) on the promoter as determined by 5'-deletion analysis. Furthermore, the activity of an SF1 ***expression*** plasmid on an SF1-dependent reporter plasmid was compromised in mutant clones. The site-specific DNA binding properties of SF1 from parent and mutant cells did not differ as determined in electrophoretic mobility shift assays, and the addition of the activation domain of VP16 to the amino terminus of SF1 restored the transcriptional activity of the protein. In addition, the levels of SF1 and other cofactors including WT1, CBP/p300, and steroid receptor coactivator 1 did not differ appreciably between parent and mutant cells. Taken together, these results suggest that ACTH resistance in the mutant clones resulted from a defect that affected the activation properties of SF1 rather than its DNA binding activity. Consistent with the observed impairment in SF1 function, other SF1-dependent genes, including Cyp11b1 and steroidogenic acute regulatory protein (StAR), were poorly expressed and global steroidogenesis, as evidenced by the metabolism of 22(R)-hydroxycholesterol to steroid products, was impaired. Interestingly, MC2R, Cyp11a, Cyp11b1, and StAR transcripts were not affected to the same degree, suggesting that each of these genes may have a different absolute requirement for SF1. These mutants thus provide an experimental paradigm to identify factors that influence SF1 function and to evaluate the relative importance of SF1 in the ***expression*** of genes essential for adrenal steroidogenesis.

L3 ANSWER 4 OF 21 MEDLINE
ACCESSION NUMBER: 2000150564 MEDLINE
DOCUMENT NUMBER: 20150564 PubMed ID: 10687856
TITLE: ***Expression*** and regulation of melanocortin receptor-5 (***MC5*** - ***R***) in the bovine adrenal cortex.
AUTHOR: Liakos P; Chambaz E M; Feige J J; Defaye G
CORPORATE SOURCE: INSERM Unite 244, CEA, Department of Molecular and Structural Biology, Grenoble, France.

SOURCE: MOLECULAR AND CELLULAR ENDOCRINOLOGY, (2000 Jan 25) 159 (1-2) 99-107.
Journal code: E69; 7500844. ISSN: 0303-7207.
PUB. COUNTRY: Ireland
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200004
ENTRY DATE: Entered STN: 20000427
Last Updated on STN: 20000427
Entered Medline: 20000418

AB Among the five members of the melanocortin receptor (MC-R) family, MC2 and MC5 are expressed in peripheral tissues. The receptor MC2 (ACTH receptor) almost exclusively expressed in the adrenal cortex whereas ***MC5*** - ***R*** is expressed in several organs including the adrenal cortex. Both receptors bind ACTH and activate adenylate cyclase. The aim of this work was to study the spatial distribution of ***MC5*** - ***R*** among the different zones of the bovine adrenal cortex and to analyze the regulation of its ***expression*** by its own ligands, ACTH and alpha-MSH and by angiotensin II (AII). Using semi-quantitative reverse transcriptase-polymerase chain reaction (RT-PCR) analysis and RNase protection assay, ***MC5*** - ***R*** was detected only in the glomerulosa zone whereas ***MC2*** - ***R*** was present in both glomerulosa and fasciculata zones of adult adrenal cortex. Treatments by ACTH, alpha-MSH, or AII increased the ***MC5*** - ***R*** mRNA level in glomerulosa cells by factors 7, 5, and 4.5, respectively. However, although potentially regulated by hormones, ***MC5*** - ***R*** is expressed at a level at least 100 times less than ***MC2*** - ***R*** , suggesting that ***MC5*** - ***R*** ***expression*** might only be at trace levels in grown adults, but could be much higher during embryogenesis.

L3 ANSWER 5 OF 21 MEDLINE
ACCESSION NUMBER: 2000174638 MEDLINE
DOCUMENT NUMBER: 20174638 PubMed ID: 10711496
TITLE: Species-dependent pharmacological properties of the ***melanocortin*** - ***5*** ***receptor*** .
AUTHOR: Huang R R; Singh G; Van der Ploeg L H; Fong T M
CORPORATE SOURCE: Department of Obesity Research, Merck Research Laboratories, Rahway, NJ 07065, USA.
SOURCE: JOURNAL OF RECEPTOR AND SIGNAL TRANSDUCTION RESEARCH, (2000 Jan) 20 (1) 47-59.
Journal code: CCU; 9509432. ISSN: 1079-9893.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200003
ENTRY DATE: Entered STN: 20000330
Last Updated on STN: 20000330
Entered Medline: 20000323

AB The genes encoding the melanocortin-3 receptor and ***melanocortin*** - ***5*** ***receptor*** have been cloned from rhesus monkey. Heterologous ***expression*** in CHO cells indicated species dependent in vitro pharmacological properties for the human and rhesus

melanocortin - ***5*** ***receptors*** . Several peptides including NDP-alpha-MSH, alpha-MSH, MT-II and ACTH1-24 are more potent at the rhesus ***melanocortin*** - ***5*** ***receptor*** than the human ***melanocortin*** - ***5*** ***receptor*** by more than 10-fold. In contrast, we found no species difference in pharmacological properties between the human and rhesus melanocortin-3 receptors. Such a species-dependent pharmacological difference for ***melanocortin*** - ***5*** ***receptor*** appears to be an exception compared to other G protein-coupled receptors from human and rhesus monkey.

L3 ANSWER 6 OF 21 MEDLINE
ACCESSION NUMBER: 2001069504 MEDLINE
DOCUMENT NUMBER: 20525400 PubMed ID: 11071848
TITLE: alpha-Melanocyte stimulating hormone acts as a selective inducer of secretory functions in human mast cells.
AUTHOR: Grutzkau A; Henz B M; Kirchhof L; Luger T; Artuc M
CORPORATE SOURCE: Experimental Dermatology, Charite, Campus Virchow-Klinikum, Medizinische Fakultat der Humboldt Universitat zu Berlin, Augustenburger Platz 1, 13353 Berlin, Germany..
andreas.gruetzkau@charite.de
SOURCE: BIOCHEMICAL AND BIOPHYSICAL RESEARCH COMMUNICATIONS, (2000 Nov 11) 278 (1) 14-9.
Journal code: 9Y8. ISSN: 0006-291X.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200101
ENTRY DATE: Entered STN: 20010322
Last Updated on STN: 20010322
Entered PubMed: 20001204
Entered Medline: 20010104
AB In the present study, we have investigated the pro-opiomelanocortin (POMC)-derived neuropeptide alpha-MSH for its ability to modulate activation of human mast cells. The in vitro ability of purified human skin mast cells to secrete various types of mast cell mediators was monitored in response to alpha-MSH at the mRNA and at the protein level. Picomolar concentrations of alpha-MSH induced a dose-dependent release of histamine from isolated human skin mast cells and from skin punch biopsies. However, no effect of alpha-MSH was seen regarding the ***expression*** of IL-1, IL-6, IL-8, TGF-beta, and TNF-alpha. Melanocortin receptor MC-1 was identified at the transcriptional level by RT-PCR analysis but not at the protein level, whereas, in leukemic human mast cells (HMC-1), the mRNAs and the proteins for the MC-1 and MC-5 receptor were identified. These results suggest that alpha-MSH may selectively induce acute inflammatory effects via secretion of histamine. Copyright 2000 Academic Press.

L3 ANSWER 7 OF 21 MEDLINE
ACCESSION NUMBER: 1999371276 MEDLINE
DOCUMENT NUMBER: 99371276 PubMed ID: 10443676
TITLE: Functional characterization of naturally occurring mutations of the human adrenocorticotropin receptor: poor correlation of phenotype and genotype.
AUTHOR: Elias L L; Huebner A; Pullinger G D; Mirtella A; Clark A J
CORPORATE SOURCE: Department of Chemical Endocrinology, St. Bartholomew's and

the Royal London School of Medicine and Dentistry, United Kingdom.
SOURCE: JOURNAL OF CLINICAL ENDOCRINOLOGY AND METABOLISM, (1999 Aug) 84 (8) 2766-70.
Journal code: HRB; 0375362. ISSN: 0021-972X.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 199908
ENTRY DATE: Entered STN: 19990827
Last Updated on STN: 19990827
Entered Medline: 19990819
AB Several missense mutations of the ACTH receptor (***MC2*** - ***R***) gene have been associated with the autosomal recessive syndrome of familial glucocorticoid deficiency. Attempts to demonstrate the functional role of these mutations have been confounded by difficulties in ***expression*** of the cloned receptor in cells lacking endogenous melanocortin receptors. The Y6 cell line, a mutant derived from the Y1 cell line, lacks any endogenous ***MC2*** - ***R*** and can be used for this purpose. We demonstrate that several ***MC2*** - ***R*** mutations associated with familial glucocorticoid deficiency result in an impaired maximal cAMP response (S74I, I44M, R146H) or loss of sensitivity for cAMP generation (D103N, R128C, T159K) compared to the wild-type receptor. Considerable variation in clinical phenotype exists even for patients with identical mutations of the ***MC2*** - ***R*** , and correlation between the estimated severity of the receptor defect in vitro and the age at clinical presentation and degree of clinical severity, as judged by basal and stimulated plasma cortisol concentration, is poor.

L3 ANSWER 8 OF 21 MEDLINE
ACCESSION NUMBER: 2000276642 MEDLINE
DOCUMENT NUMBER: 20276642 PubMed ID: 10816667
TITLE: ***Expression*** of MC1- and MC5-receptors on the human mast cell line HMC-1.
AUTHOR: Artuc M; Grutzkau A; Luger T; Henz B M
CORPORATE SOURCE: Department of Dermatology, Charite, Humboldt University, Berlin, Germany.
SOURCE: ANNALS OF THE NEW YORK ACADEMY OF SCIENCES, (1999 Oct 20) 885 364-7.
Journal code: 5NM; 7506858. ISSN: 0077-8923.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200006
ENTRY DATE: Entered STN: 20000616
Last Updated on STN: 20000616
Entered Medline: 20000602

L3 ANSWER 9 OF 21 MEDLINE
ACCESSION NUMBER: 2000162418 MEDLINE
DOCUMENT NUMBER: 20162418 PubMed ID: 10698592
TITLE: ACTH resistance syndromes.
AUTHOR: Huebner A; Elias L L; Clark A J
CORPORATE SOURCE: Children's Hospital, Technical University Dresden, Germany.

SOURCE: JOURNAL OF PEDIATRIC ENDOCRINOLOGY AND METABOLISM, (1999 Apr) 12 Suppl 1 277-93. Ref: 108
Journal code: CEF; 9508900.
PUB. COUNTRY: ENGLAND: United Kingdom
Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200003
ENTRY DATE: Entered STN: 20000327
Last Updated on STN: 20000327
Entered Medline: 20000310

AB Inherited adrenocorticotropin (ACTH) insensitivity syndromes comprise a group of rare diseases in which resistance to ACTH is either the sole feature or associated with other symptoms. This review focuses on two autosomal recessive disorders, familial glucocorticoid deficiency (FGD) (MIM*202200) and the triple A syndrome (MIM*231550), which have at least three different molecular aetiologies. In FGD, several missense mutations within the coding region of the ACTH receptor (***MC2*** - ***R***) have been identified in some, but not all patients, and segregation analyses and functional studies in a Y6 cell ***expression*** system confirmed that these mutations cause the disease. Some cases of FGD are not linked to the ***MC2*** - ***R*** locus on chromosome 18p11.2 suggesting genetic heterogeneity. The triple A syndrome is clinically characterized by the triad of adrenal insufficiency, achalasia and alacrima and a variety of neurological symptoms. After excluding several candidate genes we mapped this syndrome to a 6 cM interval on chromosome 12q13 with no indication for genetic heterogeneity. The identification of the gene(s) causing FGD without mutations in the ***MC2*** - ***R*** and causing the triple A syndrome may reveal novel aspects in cell signalling and neuroendocrinology.

L3 ANSWER 10 OF 21 MEDLINE
ACCESSION NUMBER: 1999158537 MEDLINE
DOCUMENT NUMBER: 99158537 PubMed ID: 10051228
TITLE: Melanocortin-4 receptor messenger RNA ***expression*** is up-regulated in the non-damaged striatum following unilateral hypoxic-ischaemic brain injury.
AUTHOR: Mountjoy K G; Guan J; Elia C J; Sirimanne E S; Williams C E
CORPORATE SOURCE: Department of Paediatrics, University of Auckland, New Zealand.
SOURCE: NEUROSCIENCE, (1999 Mar) 89 (1) 183-90.
Journal code: NZR; 7605074. ISSN: 0306-4522.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199904
ENTRY DATE: Entered STN: 19990511
Last Updated on STN: 20000303
Entered Medline: 19990426

AB Melanocortin peptides (alpha-melanocyte-stimulating hormone, adrenocorticotropin and fragments thereof) have been shown to have numerous effects on the central nervous system, including recovery from nerve injury and retention of learned behaviour, but the mechanism of

action of these peptides is unknown. A family of five melanocortin receptors have recently been discovered, two of which (melanocortin-3 and melanocortin-4 receptors) have been mapped in the rat brain. We have tested the hypothesis that the ***expression*** of one or more of the messenger RNAs for three melanocortin receptors (melanocortin-3, melanocortin-4 and ***melanocortin*** - ***5*** ***receptors***) would be altered in rat brain following unilateral transient hypoxic-ischaemic brain injury. In this study, using in situ hybridization, we show that melanocortin-4 receptor messenger RNA was up-regulated in the striatum in the non-damaged hemisphere within 24 h after severe hypoxic-ischaemic injury compared with control brains ($P<0.05$). In a small group of animals, this induction was not blocked by treatment with the anticonvulsant, carbamazepine. ***Expression*** of melanocortin-3 receptor messenger RNA in the brain was not altered in this hypoxic-ischaemic injury model and ***melanocortin*** - ***5*** ***receptor*** messenger RNA was not detected in either control or hypoxic-ischaemic injured rat brains. We hypothesize that the up-regulation of melanocortin-4 receptor messenger RNA ***expression*** in the contralateral striatum may be involved in transfer of function to the uninjured hemisphere following unilateral brain injury.

L3 ANSWER 11 OF 21 MEDLINE
ACCESSION NUMBER: 1998224515 MEDLINE
DOCUMENT NUMBER: 98224515 PubMed ID: 9564844
TITLE: ***Expression*** of ***melanocortin*** - ***5*** ***receptor*** in secretory epithelia supports a functional role in exocrine and endocrine glands.
AUTHOR: van der Kraan M; Adan R A; Entwistle M L; Gispen W H; Burbach J P; Tatro J B
CORPORATE SOURCE: Rudolf Magnus Institute for Neurosciences, Department of Medical Pharmacology, Utrecht University, The Netherlands.
CONTRACT NUMBER: MH-44694 (NIMH)
SOURCE: ENDOCRINOLOGY, (1998 May) 139 (5) 2348-55.
Journal code: EGZ; 0375040. ISSN: 0013-7227.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 199805
ENTRY DATE: Entered STN: 19980520
Last Updated on STN: 19980520
Entered Medline: 19980508

AB Melanocortins (alphaMSH and ACTH-related peptides) influence the physiological functions of certain peripheral organs, including exocrine and endocrine glands. This study was designed to determine the identity and anatomical localization of the melanocortin receptors (MC-R) expressed in these organs in the rat. ***MC5*** - ***R*** messenger RNA was found in exocrine glands, including lacrimal, Harderian, preputial, and prostate glands and pancreas, as well as in adrenal gland, esophagus, and thymus, as demonstrated by ribonuclease protection assays. In exocrine glands, ***MC5*** - ***R*** messenger RNA ***expression*** was restricted to secretory epithelia. MC-R protein was likewise present in secretory epithelia of exocrine glands, as determined by 125I-labeled [Nle4,D-Phe7]alphaMSH ([125I]NDP-MSH) binding and autoradiography in tissue sections. Specific [125I]NDP-MSH binding was also observed in adrenal cortex, thymus, spleen, and esophageal and trachealis muscle. MC

receptors in these sites are accessible to circulating MC-R agonists in vivo, as specific binding of [125I]NDP-MSH was observed in exocrine and adrenal glands after systemic injection in vivo. Taken together, these findings show that the MC5 receptor is commonly and selectively expressed in exocrine glands and other peripheral organs. Based on these findings and compelling evidence from other studies, a functional coherence is suggested between central and peripheral actions of melanocortins and melanocortin receptors in physiological functions, including thermoregulation, immunomodulation, and sexual behavior.

L3 ANSWER 12 OF 21 MEDLINE
ACCESSION NUMBER: 1999103595 MEDLINE
DOCUMENT NUMBER: 99103595 PubMed ID: 9888520
TITLE: ***Expression*** of ACTH receptors (***MC2*** - ***R*** and ***MC5*** - ***R***) in the glomerulosa and the fasciculata-reticularis zones of bovine adrenal cortex.
AUTHOR: Liakos P; Chambaz E M; Feige J J; Defaye G
CORPORATE SOURCE: CEA, INSERM U. 244, DBMS, Grenoble, France.
SOURCE: ENDOCRINE RESEARCH, (1998 Aug-Nov) 24 (3-4) 427-32.
Journal code: EIH; 8408548. ISSN: 0743-5800.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199904
ENTRY DATE: Entered STN: 19990426
Last Updated on STN: 19990426
Entered Medline: 19990413
AB The recent cloning of a family of melanocortin receptors (MC-R) has identified five distinct G protein- and adenylate cyclase-coupled receptors. The MC2-receptor (***MC2*** - ***R***) preferentially binds ACTH. It is expressed in the adrenal cortex and is hence considered to be the ACTH receptor. The MC5-receptor (***MC5*** - ***R***) binds ACTH and alpha-MSH and is more widely expressed. The aim of this work was to study the sites of ***MC5*** - ***R*** ***expression*** in the bovine adrenal cortex and to compare the regulation of the ***expression*** of ***MC2*** - ***R*** and ***MC5*** - ***R*** in bovine adrenocortical cells in primary culture. Analysis of the ***expression*** of ***MC5*** - ***R*** was obtained by RT-PCR, using total RNA purified from glomerulosa and fasciculata zones of bovine adrenocortical tissue. ***MC5*** - ***R*** ***expression*** could be detected in RNA from the glomerulosa zone but was undetectable in the fasciculata zone. In bovine adrenocortical cells in culture, ACTH stimulates ***MC5*** - ***R*** ***expression*** in the glomerulosa and fasciculata cells. A DNA fragment, was obtained using primers based on the bovine ACTH receptor (***MC2*** - ***R***) sequence. This fragment was detected in RNA from the two zones. The probe was used to quantify ***MC2*** - ***R*** by Ribonuclease Protection assay and we observed that ***MC2*** - ***R*** mRNA is 3.6-fold more abundant in glomerulosa than in fasciculata-reticularis cells.

L3 ANSWER 13 OF 21 MEDLINE
ACCESSION NUMBER: 1999003060 MEDLINE
DOCUMENT NUMBER: 99003060 PubMed ID: 9784305

TITLE: Melanocortin receptor genes in the chicken--tissue distributions.
AUTHOR: Takeuchi S; Takahashi S
CORPORATE SOURCE: Faculty of Science, Okayama University, Okayama, 700-8530, Japan.. stakeuch@cc.okayama-u.ac.jp
SOURCE: GENERAL AND COMPARATIVE ENDOCRINOLOGY, (1998 Nov) 112 (2) 220-31.
Journal code: FL9; 0370735. ISSN: 0016-6480.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199812
ENTRY DATE: Entered STN: 19990115
Last Updated on STN: 19990115
Entered Medline: 19981217

AB Two receptor genes belonging to the melanocortin receptor (MC-R) family were isolated in the chicken, the CMC4 and CMC5, each of which is a chicken homologue of the mammalian MC4-R and ***MC5*** - ***R*** , respectively. The CMC4 encodes a 331 amino acid protein, sharing 86.4-88.1% identity with mammalian analogs, and the CMC5 encodes a 325 amino acid protein, which is 72.3-79.1% identical to mammalian counterparts. Both genes contain no intron in their coding regions and exist in the chicken genome as single copy genes. Reverse transcription-PCR analysis revealed that the CMC4 mRNA is expressed in a wide variety of peripheral tissues, including the adrenal, gonads, spleen, and adipose tissues, as well as in the brain, where mammalian counterparts are exclusively expressed in the brain, indicating that the regulation of MC4-R gene ***expression*** differs between mammals and chickens. The CMC5 mRNA, on the other hand, is expressed in the liver, gonads, adrenal, kidney, brain, and adipose tissues as well as in the uropygial gland. These findings raise the possibility that melanocortins affect a variety of functions both in the brain and in the peripheral tissues of the chicken.
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L3 ANSWER 14 OF 21 MEDLINE
ACCESSION NUMBER: 1998053491 MEDLINE
DOCUMENT NUMBER: 98053491 PubMed ID: 9392003
TITLE: Linkage and association studies between the melanocortin receptors 4 and 5 genes and obesity-related phenotypes in the Quebec Family Study.
AUTHOR: Chagnon Y C; Chen W J; Perusse L; Chagnon M; Nadeau A; Wilkison W O; Bouchard C
CORPORATE SOURCE: Physical Activity Sciences Laboratory, Laval University, Ste-Foy, Quebec, Canada.
CONTRACT NUMBER: 1P41RR03655 (NCRR)
SOURCE: MOLECULAR MEDICINE, (1997 Oct) 3 (10) 663-73.
Journal code: CG3; 9501023. ISSN: 1076-1551.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199801
ENTRY DATE: Entered STN: 19980217
Last Updated on STN: 19980217
Entered Medline: 19980130

AB BACKGROUND: The agouti yellow mouse shows adult onset of moderate obesity and diabetes. A depressed basal lipolytic rate in adipocytes or a decreased adrenergic tone arising from antagonizing alpha-melanocyte-stimulating hormone (MSH) activation of melanocortin receptors (MCR) could be at the origin of the obesity phenotype. MATERIAL AND METHODS: MCR 4 and 5 (MC4R, MC5R) genes were studied in the Quebec Family Study. Sequence variations were detected by Southern blot probing of restricted genomic DNA, and mRNA tissue ***expression*** was detected by RT-PCR. Subjects with a wide range of weight were used for single-point sib-pair linkage studies (maximum of 289 sibships from 124 nuclear families). Analysis of variance across genotypes in unrelated males (n = 143) and females (n = 156) was also undertaken. Body mass index (BMI), sum of six skin-folds (SF6), fat mass (FM), percent body fat (%FAT), respiratory quotient (RQ), resting metabolic rate (RMR), fasting glucose and insulin, and glucose and insulin area during an oral glucose tolerance test were analyzed. RESULTS: MC4R showed polymorphism with NcoI, and MC5R, with PstI and PvuII, with a heterozygosity of 0.38, 0.10, and 0.20, respectively. Linkages were observed between MC5R and BMI (p = 0.001), SF6 (p = 0.005), FM (p = 0.001), and RMR (p = 0.002), whereas associations were observed in females between MC5R and BMI (p = 0.003), and between MC4R and FM (p = 0.002) and %FAT (p = 0.004). After correction for multiple tests, these p values are lowered by one tenth. MC4R and MC5R mRNAs have been detected in brain, adipose tissue, and skeletal muscle. CONCLUSIONS: MC4R and MC5R exhibit evidence of linkage or association with obesity phenotypes, but this evidence is strongest for MC5R.

L3 ANSWER 15 OF 21 MEDLINE
ACCESSION NUMBER: 97160908 MEDLINE
DOCUMENT NUMBER: 97160908 PubMed ID: 9008228
TITLE: Production of POMC, CRH-R1, MC1, and MC2 receptor mRNA and ***expression*** of tyrosinase gene in relation to hair cycle and dexamethasone treatment in the C57BL/6 mouse skin.
AUTHOR: Ermak G; Slominski A
CORPORATE SOURCE: Department of Pathology and Laboratory Medicine, Albany Medical College, New York 12208, USA.
SOURCE: JOURNAL OF INVESTIGATIVE DERMATOLOGY, (1997 Feb) 108 (2) 160-5.
Journal code: IHZ; 0426720. ISSN: 0022-202X.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199702
ENTRY DATE: Entered STN: 19970227
Last Updated on STN: 19970227
Entered Medline: 19970213

AB In skin of the C57BL/6 mouse, the production of mRNA transcripts that hybridized to the coding region of the MC1 receptor (MC1-R) gene was undetectable in telogen, increased during hair growth, and, after reaching the highest values in anagen VI, decreased during the anagen-catagen transition phase. This production was associated with anagen-dependent ***expression*** of the tyrosinase gene and enzyme activity. In contrast, the production of 4.5- and 2.0-kb mRNAs hybridizable to the coding region of the MC2 receptor (***MC2*** - ***R***) gene was similar throughout the entire hair cycle. Previously, dexamethasone was

demonstrated to induce premature catagen development accompanied by an abrupt termination of melanogenesis. Here we demonstrate that topical application of dexamethasone during anagen VI decreased the concentration of POMC, MC1-R, and tyrosinase mRNA in the skin. The decrease in tyrosinase mRNA concentration was accompanied by a decrease in tyrosinase protein concentration and enzyme activity. These results support the hypothesis that murine hair growth and attendant melanogenesis can be regulated through coordinated changes in local ***expression*** of POMC, MC1-R, and tyrosinase genes.

L3 ANSWER 16 OF 21 MEDLINE
ACCESSION NUMBER: 96387362 MEDLINE
DOCUMENT NUMBER: 96387362 PubMed ID: 8794897
TITLE: Morphine down-regulates melanocortin-4 receptor ***expression*** in brain regions that mediate opiate addiction.
AUTHOR: Alvaro J D; Tatro J B; Quillan J M; Fogliano M; Eisenhard M; Lerner M R; Nestler E J; Duman R S
CORPORATE SOURCE: Laboratory of Molecular Psychiatry, Yale University School of Medicine, New Haven, Connecticut 06508, USA.
CONTRACT NUMBER: DA08227 (NIDA)
MH44694 (NIMH)
SOURCE: MOLECULAR PHARMACOLOGY, (1996 Sep) 50 (3) 583-91.
Journal code: NGR; 0035623. ISSN: 0026-895X.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
OTHER SOURCE: GENBANK-U67863
ENTRY MONTH: 199610
ENTRY DATE: Entered STN: 19961219
Last Updated on STN: 19980206
Entered Medline: 19961031

AB Melanocortin peptides are reported to antagonize opiate dependence and tolerance, but the neural substrates underlying these actions are unknown. In this study, we characterize the rat melanocortin-4 receptor (MC4-R) and demonstrate that this receptor is regulated by opiate administration. The rat MC4-R is 95% identical to the human MC4-R, and the potency of melanocortin peptides to stimulate cAMP production is similar in these two species homologs (alpha-melanocyte-stimulating hormone = adrenocorticotropic hormone > gamma-melanocyte-stimulating hormone). ***Expression*** of MC4-R mRNA was found to be enriched in the striatum, nucleus accumbens, and periaque-ductal gray, all of which are regions implicated in the behavioral effects of opiates. In contrast, MC1-, MC3-, and ***MC5*** - ***R*** are expressed at very low or undetectable levels in these brain regions. Chronic administration of morphine (5 days) resulted in a time-dependent down-regulation of MC4-R mRNA ***expression*** in the striatum and periaqueductal gray. ***Expression*** of MC4-R mRNA was also decreased in the nucleus accumbens/ olfactory tubercle, but this effect was observed after 1 or 3 days of morphine treatment. In the striatum, the reduction of MC4-R mRNA was accompanied by a concomitant decrease in melanocortin receptor levels, shown by quantitative radioligand binding and autoradiography. In contrast, morphine administration did not influence levels of MC4-R mRNA in several other brain regions, including frontal cortex, olfactory bulb, hypothalamus, and ventral tegmentum/substantia nigra. In light of previous

findings that melanocortins antagonize opiate self-administration, analgesic tolerance, and physical dependence, we hypothesize that decreased melanocortin function, via down-regulation of MC4-R ***expression*** , may contribute to the development of these opiate-induced behaviors.

L3 ANSWER 17 OF 21 MEDLINE
ACCESSION NUMBER: 96233816 MEDLINE
DOCUMENT NUMBER: 96233816 PubMed ID: 9011763
TITLE: Melanocortin receptors mediate alpha-MSH-induced stimulation of neurite outgrowth in neuro 2A cells.
AUTHOR: Adan R A; van der Kraan M; Doornbos R P; Bar P R; Burbach J P; Gispen W H
CORPORATE SOURCE: Rudolf Magnus Institute for Neurosciences, Department of Medical Pharmacology, Utrecht University, The Netherlands.
SOURCE: BRAIN RESEARCH. MOLECULAR BRAIN RESEARCH, (1996 Feb) 36 (1) 37-44.
Journal code: MBR; 8908640. ISSN: 0169-328X.
PUB. COUNTRY: Netherlands
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199702
ENTRY DATE: Entered STN: 19970219
Last Updated on STN: 19970219
Entered Medline: 19970206
AB Melanocortins (MC), neuropeptides derived from pro-opiomelanocortin, have been implicated in enhancing neurite outgrowth via an as yet unknown mechanism. Recently, five MC receptors have been identified, three of which, the MC3-R, the MC4-R and the ***MC5*** - ***R*** , are expressed in the nervous system. In this study, alpha-MSH and the melanocortin analog [D-Phe7]ACTH (4-10) were able to stimulate neurite outgrowth in the neuroblastoma cell line Neuro 2A. ACTH (4-10), gamma2-MSH and ORG2766 were inactive. In addition, the MC4-R antagonist [D-Arg8]ACTH (4-10), inhibited the alpha-MSH effect, indicating that the MC4-R mediated stimulation of neurite outgrowth by alpha-MSH. Indeed, the presence of MC4-R mRNA in Neuro 2A cells was demonstrated by a RNase protection assay. Heterologous ***expression*** of the ***MC5*** - ***R*** in Neuro 2A cells lead to the recruitment of a responsiveness to gamma2-MSH, but did not increase the effect of alpha-MSH on neurite outgrowth. This finding indicated that the function of MC4-R can also be exerted by another MC receptor, suggesting that the coupling to Gs, which they have in common, plays an essential role in the neurite outgrowth promoting effect. This was further substantiated by the fact that forskolin treatment per se induced neurite outgrowth in a similar fashion. These data imply that the neurotrophic properties of alpha-MSH are likely to result from Gs-coupled MC receptor activity in neuronal cells.

L3 ANSWER 18 OF 21 MEDLINE
ACCESSION NUMBER: 94213827 MEDLINE
DOCUMENT NUMBER: 94213827 PubMed ID: 8161509
TITLE: Molecular cloning of a mouse ***melanocortin*** ***5*** ***receptor*** gene widely expressed in peripheral tissues.
AUTHOR: Labbe O; Desarnaud F; Eggerickx D; Vassart G; Parmentier M
CORPORATE SOURCE: Institut de Recherche Interdisciplinaire en Biologie

Humaine et Nucleaire, Universite Libre de Bruxelles, Belgium.
SOURCE: BIOCHEMISTRY, (1994 Apr 19) 33 (15) 4543-9.
Journal code: A0G; 0370623. ISSN: 0006-2960.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
OTHER SOURCE: GENBANK-X76295
ENTRY MONTH: 199405
ENTRY DATE: Entered STN: 19940606
Last Updated on STN: 19940606
Entered Medline: 19940526

AB A mouse genomic clone named HGMP01B has been isolated by homology screening with a probe representing part of the human melanocortin 3 receptor gene. HGMP01B was found to encode a 325 amino acid protein with all the landmarks of G-protein-coupled receptors and belonging to the growing melanocortin receptor family. This receptor displays four potential sites for N-linked glycosylation and five potential sites of phosphorylation by protein kinase C. The HGMP01B gene was found to be expressed in many tissues, including skin, adrenal gland, skeletal muscle, bone marrow, spleen, thymus, gonads, uterus, and brain. A stable Chinese hamster ovary (CHO) cell line expressing approximately 10,000 receptors per cell was established. This cell line displayed a saturable binding capacity for the radioiodinated alpha-melanocyte-stimulating hormone (alpha-MSH) analog [Nle4,D-Phe7]-alpha-MSH (NDP-MSH) with an apparent Kd of 1.47 +/- 0.15 nM. Binding of the labeled ligand was competed for by all melanocortin peptides, except beta-endorphin or corticotropin-like intermediate lobe peptide (CLIP). NDP-MSH was the most powerful competitor, followed by alpha-MSH, adrenocorticotropic hormone (ACTH), beta-MSH, the gamma-MSHs, and ACTH 4-10. Functional assays confirmed that HGMP01B, like other melanocortin receptors, stimulated adenylyl cyclase. The potency order obtained in these cyclic adenosine monophosphate (cAMP) accumulation assays was consistent with that of the binding studies. HGMP01B therefore appears as a fifth melanocortin receptor (MC5), responding mainly to alpha-MSH (EC50 = 1.07 +/- 0.13 nM) and endowed with a pharmacological profile similar to that of the melanocyte MSH (MC1) receptor, but characterized by a broad tissue distribution.(ABSTRACT TRUNCATED AT 250 WORDS)

L3 ANSWER 19 OF 21 MEDLINE
ACCESSION NUMBER: 94241974 MEDLINE
DOCUMENT NUMBER: 94241974 PubMed ID: 8185570
TITLE: Molecular cloning, ***expression*** , and characterization of a fifth melanocortin receptor.
AUTHOR: Gantz I; Shimoto Y; Konda Y; Miwa H; Dickinson C J; Yamada T
CORPORATE SOURCE: Department of Surgery, University of Michigan Medical Center, Ann Arbor.
CONTRACT NUMBER: P30-DK34933 (NIDDK)
RO1-DK33000 (NIDDK)
RO1-DK34306 (NIDDK)
+
SOURCE: BIOCHEMICAL AND BIOPHYSICAL RESEARCH COMMUNICATIONS, (1994 May 16) 200 (3) 1214-20.
Journal code: 9Y8; 0372516. ISSN: 0006-291X.

PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
OTHER SOURCE: GENBANK-L22527
ENTRY MONTH: 199406
ENTRY DATE: Entered STN: 19940621
Last Updated on STN: 19970203
Entered Medline: 19940616

AB We report the isolation of a gene encoding a novel member of the family of melanocortin receptors. The mouse ***melanocortin*** - ***5*** ***receptor*** (mMC5R) responds to melanocortins with an increase in intracellular cyclic 3',5'-adenosine monophosphate (cAMP) concentrations. Stimulation of the mMC5R by the melanocortins revealed a hierarchy of potency in which alpha-melanocyte stimulating hormone (alpha-MSH) > beta-melanocyte stimulating hormone (beta-MSH) > adrenocorticotropic hormone (ACTH) > gamma- melanocyte stimulating hormone (gamma-MSH). Further structure-activity studies indicated that amino- and carboxyl-terminal portions of alpha-MSH appear to be key determinants in the activation of mMC5R whereas the melanocortin core heptapeptide sequence is devoid of pharmacological activity. Northern blot analysis demonstrated the ***expression*** of mMC5R mRNA in mouse skeletal muscle, lung, spleen, and brain.

L3 ANSWER 20 OF 21 MEDLINE
ACCESSION NUMBER: 94234987 MEDLINE
DOCUMENT NUMBER: 94234987 PubMed ID: 8179577
TITLE: Molecular cloning and characterization of the rat fifth melanocortin receptor.
AUTHOR: Griffon N; Mignon V; Facchinetti P; Diaz J; Schwartz J C; Sokoloff P
CORPORATE SOURCE: Unite de Neurobiologie et Pharmacologie de l'INSERM, Centre Paul Broca, Paris, France.
SOURCE: BIOCHEMICAL AND BIOPHYSICAL RESEARCH COMMUNICATIONS, (1994 Apr 29) 200 (2) 1007-14.
Journal code: 9Y8; 0372516. ISSN: 0006-291X.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
OTHER SOURCE: GENBANK-L27080; GENBANK-L27081
ENTRY MONTH: 199406
ENTRY DATE: Entered STN: 19940620
Last Updated on STN: 19940620
Entered Medline: 19940603

AB Adrenocorticotropic hormone (ACTH) and melanocortin peptides (alpha, beta and gamma MSH) have numerous activities in both central nervous system and peripheral tissues, namely the adrenals. Recently, five melanocortin receptors were cloned and characterized. We report here the cloning, pharmacological characterization and ***expression*** of the rat fifth melanocortin receptor (MC5), starting from the dopamine D3 receptor sequence to screen a genomic DNA library. The MC5 comprises a sequence of 325 amino acids, displaying 45-62% identity with other melanocortin receptors and 82% identity with its human counterpart that we cloned thereafter. The sequence of the latter is identical to that of a so-called 'MC2' receptor (Chhajlani et al., 1993, Biochem. Biophys. Res. Comm. 195,

866-873). The MC5, stably expressed in CHO cells, mediates increase in cAMP accumulation with a characteristic pharmacology: alpha MSH is twice as potent as NDP alpha MSH, 10 times as ACTH and 100 times as gamma MSH. Very low ***expression*** levels were detected in brain, while high levels were found in adrenals, stomach, lung and spleen. In addition, in situ hybridization studies show the MC5 expressed in the three layers of the adrenal cortex, predominantly in the aldosterone-producing zona glomerulosa cells.

L3 ANSWER 21 OF 21 MEDLINE
ACCESSION NUMBER: 94076637 MEDLINE
DOCUMENT NUMBER: 94076637 PubMed ID: 8254933
TITLE: Adrenocorticotropin receptor in familial glucocorticoid deficiency.
AUTHOR: Takayanagi R; Sakai Y; Nawata H; Nishiyama S; Ito T; Kodama M; Matsuda I; Matsuda H
CORPORATE SOURCE: Third Department of Internal Medicine, Faculty of Medicine, Kyushu University.
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AB Recent studies have revealed the presence of four subtypes for the melanocortin receptor (MC-R). Among these MC-Rs, ***MC2*** - ***R*** is considered to be an adrenocorticotropin (ACTH) receptor because its ***expression*** is almost localized in the adrenal cortex. Five Japanese patients with ACTH unresponsiveness were examined as to whether they have mutations in the putative ACTH receptor. Among these patients, there are two groups of siblings, each of which consists of two individuals. The coding region of the ACTH receptor gene was amplified by polymerase chain reaction and directly sequenced on both strands, however, no point mutation was found in any of the five patients, suggesting that familial glucocorticoid deficiency, caused by the mutated ACTH receptor, may be rare.